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T.D. Chinevere, J.P. McClung, S.N. Cheuvront

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Thermal and Mountain Medicine Division
U.S. Army Research Institute of Environmental Medicine
Natick, MA 01760-5007

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Trace Mineral Losses in Sweat

Troy D. Chinevere*, James P. McClung and Samuel N. Cheuvront

U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760, USA

Abstract: Copper, iron and zinc are nutritionally essential trace minerals that confer vital biological roles including the maintenance of cell structure and integrity, regulation of metabolism, immune function, oxygen transport, and muscle and central nervous system function. Dietary Reference Intakes (DRIs) for these minerals are useful for the general population, but these guidelines may be inadequate for some populations (e.g., soldiers, athletes) who experience copious sweating due to high physical activity levels and/or frequent exposure to extreme environmental conditions. The trace mineral content of sweat may predispose these populations to subclinical/clinical nutritional deficiencies. Studies on sweat trace mineral losses report highly variable results. Much of the variability may be methodological. Non-standardization of collection techniques, collection sites (local versus whole body), and numerous other variables cloud definitive conclusions on sweat trace mineral losses. The objectives of this manuscript are to 1) review the literature on sweat copper, iron, and zinc losses, 2) present the potential sources of variability, 3) interpret findings in relation to nutritional needs, and 4) identify directions for future research.

Keywords: Copper, iron, zinc, sweat rate, sweat collection.

INTRODUCTION

Regular heavy sweating from routine physical activity in hot environments may affect sweat losses of trace minerals. Over the past 50 years, trace mineral losses in sweat have been measured under a variety of conditions; however, the findings have been highly variable among studies, even under similar conditions. Variable results may be explained by a number of factors including: 1) trace mineral contamination, 2) differences among sweat collection methods and body sites, 3) the duration of the sweat collection period, and 4) the impact of physical activity and/or the environment on sweating rate. Since sweat mineral concentrations differ when comparing sweat induction techniques like pilocarpine iontophoresis and thermally-induced sweating [1], this review will focus specifically on studies using heat exposure, exercise, or the combination of exercise-heat stress to stimulate sweating. Lastly, the sweat trace mineral concentrations and losses reported in this review do not distinguish between apocrine, apoeccrine, or eccrine sweat glands. No published data exist that compare the sweat trace mineral content between the different sweat glands. However, *in vitro* studies [2] suggest that sweat sodium concentration appears to be higher in apoeccrine and apocrine sweat glands versus eccrine sweat glands with sweat rate being highest in apoeccrine sweat glands.

SWEAT TRACE MINERAL LOSSES

Copper

Copper is involved with glucose, cholesterol, and iron metabolism, cardiovascular system structure and function, immune system and oxidative defense function, and the biosynthesis of neuropeptides [3,4]. A main function of copper is activation of the enzyme ceruloplasmin which is required for iron binding to the serum transport protein transferrin. The mechanism by which copper is translocated to the surface and released in sweat is not known. To date, most research studies examining sweat copper concentrations have used a resting heat exposure paradigm. One of the earliest studies reported sweat copper concentrations of 0.058 mg/L over selected areas of the body in subjects exposed to hot, humid conditions [5]. Similar mean±SD values ranging from 0.027±0.013 – 0.12±0.10 mg/L have been reported in sweat from the arm [6,7], but other studies measuring arm sweat copper concentrations report either much higher (0.33±0.16 – 1.48±0.61 mg/L) [1,8] or lower (<0.006 mg/d) [9] values. When comparing local arm to whole body sweat copper concentration or losses, it is generally concluded [5,6] that the two are not reliably correlated.

Few studies have measured sweat copper concentrations during physical activity. Aruoma *et al.* [10] examined local sweat copper concentrations from various body regions during exercise in a temperate environment. Their findings of 0.89±0.63 mg/L (abdomen), 0.73±0.74 mg/L (chest), 0.56±0.43 mg/L (back), and 0.52±0.48 mg/L (arm) demonstrate the variability in sweat copper concentrations at different sites of the body. Omokhodion and Howard [11] later found arm sweat copper concentrations (0.49±0.19 mg/L) similar to those observed by Aruoma *et al.* [9] in exercising men. Saraymen *et al.* [12,13] reported arm sweat copper concentration values of 0.38±0.05 and 0.29±0.03 mg/L in boxers and wrestlers, respectively, following 30 min of exercise in a temperate environment. These values are also similar to those reported by some [1,8], but not all [5,6,7] resting heat exposure experiments measuring arm sweat copper concentrations.

Whether heat or exercise is used to stimulate sweating, there is wide variability in reported sweat copper concentrations and losses. This might be attributable to large inter-individual variability, different study designs, or collection methodologies. In addition, no study has demonstrated a reliable relationship between local sweat copper concentration and whole body copper concentration or losses.

Iron

Iron is responsible for binding oxygen in hemoglobin, transporting electrons within cells, and is vitally integrated within various enzyme systems [14,15]. Perhaps the best known function of iron is through its incorporation into heme-containing proteins, including hemoglobin for oxygen transport and myoglobin for muscle storage of oxygen. Iron is transported in the blood as transferrin, which binds to receptors on peripheral cells. The mechanism by which iron translocates from the plasma to the sweat gland is currently unknown. The few studies that have measured sweat iron concentration during resting heat exposure report variable findings [7,16,17]. Vellar [16] found the whole body iron concentration of cell-rich sweat to be 0.41±0.13 mg/L and the cell-free iron content to be 0.30±0.09 mg/L during a 60 minute sauna bath. Brune *et al.* [17] later reported 10-fold lower whole body sweat iron concentration values of 0.02±0.01 mg/L and 0.05±0.02 mg/L in cell-free and cell-rich sweat, respectively, using a similar sauna exposure. Hoshi *et al.* [7] compared whole body sweat to arm

*Address correspondence to this author at the U. S. Army Research Institute of Environmental Medicine, Bldg. 42, Kansas Street, Natick, MA 01760, USA; Tel: (508) 233-4598; Fax: (508) 233-5298;
E-mail: Troy.Chinevere@us.army.mil

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bag sweat iron concentrations after sauna bathing and found that whole body sweat iron concentration was significantly higher (0.03±0.02 mg/L) than arm bag sweat iron concentration (0.015 ±0.01 mg/L). However, the authors concluded that the whole body sweat iron concentration may have been contaminated with iron-containing air dust particulates and/or cellular debris.

Sweat concentrations of iron have also been measured during exercise [10,17,19,20,21]. It appears that sweat iron declines with time from early sweating onset during heat exposure or exercise [17,19,20,22] (Fig. **1**). For example, Paulev *et al.* [19] observed the clear (cell-poor) sweat iron concentration from the backs of two groups of runners to be 30% lower, but not significantly ($p<0.1$), than the unclear (cell-rich) sweat iron concentration after 30 minutes of cycle ergometry exercise. In one group, the initial, unclear sweat collection was analyzed, whereas, in the other group, the clear sweat was not collected until after the initial sweat was wiped free to minimize the number of skin cells. A ~50% reduction was found in the cell-free sweat iron concentration in 11 healthy males during 2 periods of consecutive sauna bath exposures [17]. Waller and Haymes [20] measured sweat iron concentrations in different environments collected from the arm and noted a significant decrease at 60 minutes of exercise compared with the first 30 minutes of exercise. In a hot, humid environment, the authors reported arm sweat iron concentrations of 0.21 mg/L at 30 minutes and 0.08 mg/L at 60 minutes of exercise. At 30 and 60 minutes of exercise in a temperate environment, arm sweat iron concentrations were 0.31 mg/L and 0.14 mg/L, respectively. Furthermore, the authors reported similar arm sweat iron concentrations while subjects rested in a hot, humid environment to those seen during exercise in the temperate environment. Deruisseau *et al.* [22] subsequently observed a similar trend in the sweat iron concentration during exercise as that seen by Waller and Haymes [20] (Fig. 1). Mean sweat iron concentration values were 0.19 mg/L after 30 minutes and 0.11 mg/L at 120 minutes during cycle ergometry in a temperate environment. Estimated sweat iron losses were found to be significantly lower during the second half (120 min) versus the first half (60 min) of exercise, which is in contrast to no differences for the estimated sweat iron losses observed by Waller and Haymes [20] between 30 and 60 minutes of exercise in a temperate environment. These observations may be simply due to the additional 60 minutes of exercise employed in Deruisseau *et al.* [22] study.

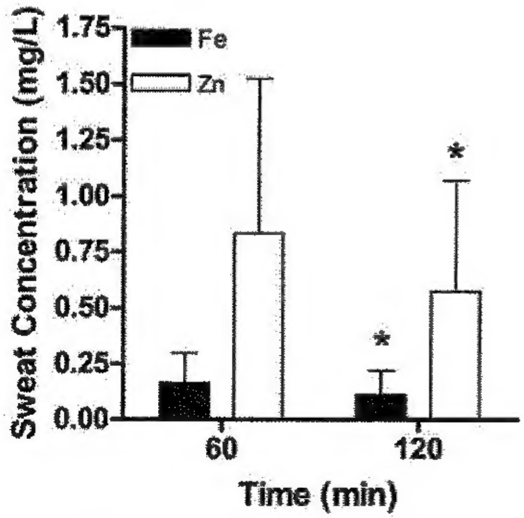

Fig. (1). Reduction in sweat iron and zinc concentrations between 60 and 120 minutes of exercise. * Significantly different from 60 minutes. Data are for male subjects only (summarized and redrawn from DeRuisseau *et al.* [22]).

Zinc

Zinc is known to be essential for the function of over 300 proteins that synthesize or degrade lipids, carbohydrates, proteins, nucleic acids, and the metabolism of other micronutrients. Whole body zinc retention is estimated to be 2-3 grams with 85-90% of the zinc retained in skeletal muscle and bone. Circulating zinc represents about 0.1% of whole body zinc, mostly bound to albumin and amino acids (~60%), with the other 40% bound to α_2-macroglobulin [23]. The physiological stimulus that releases circulating bound zinc into the sweat gland is currently not known. During heat exposure at rest, sweat zinc concentration from the torso appears substantial (41.2 mg/L) [24]. Conversely, mean sweat zinc concentration sampled from the arms of a large, healthy adult cohort (n = 48) was much lower in males (0.50±0.48 mg/L) and females (~1.20±0.70 mg/L) at rest in the heat [8].

Exercise in warm environmental conditions appears to lower zinc sweat concentration compared to exercise in cooler environments [18]. Tipton *et al.* [18] reported significantly higher arm sweat zinc concentrations after 60-min of exercise (cycle ergometry) in a temperate (0.87±0.87 mg/L) versus a hot (0.52±0.41 mg/L) environment. Similar to the decline observed in sweat iron over time during exercise, when the values for men and women were collapsed, sweat zinc concentrations decreased by ~58% during the second half of exercise in both environments, suggesting that exercise duration may impact sweat zinc concentration. A more recent study [22] observed a similar trend of declining arm sweat zinc concentration over the duration of exercise during 2 hours of cycle ergometry in a temperate environment (Fig. **1**). Arm sweat zinc concentrations were 0.90 mg/L and 0.56 mg/L during the first and second hour of exercise, respectively. A possible explanation for the zinc concentration differences between the two different environments is that the higher sweating rates dilute these losses and lower their concentration in sweat. This explanation is supported by evidence that the calculated total sweat zinc losses (mg/L x total L) were similar between the warm and cooler environments [18]. However, the sweating rates were not significantly higher at 120 min versus 60 min of exercise as measured by Deruisseau *et al.* [22], suggesting that some other mechanism, possibly trace mineral conservation, may explain the decline in sweat zinc concentration over time. In concurrence with the observations made by Tipton *et al.* [18] and DeRuisseau *et al.* [22], we have also observed a 42-45% decline in the sweat zinc concentration during 7-h of prolonged exercise-heat stress [unpublished observations].

POTENTIAL SOURCES OF SWEAT MINERAL VARIABILITY

Early studies of trace mineral concentrations and losses in sweat demonstrate considerable variability in reported concentrations for each mineral. It appears that the sweating rate induced by different environments or exercise affects sweat mineral concentrations. Thermoregulatory sweating increases proportionately with the total thermal load [25], and experiments that incorporate both temperate and hot environments all show differences in the sweating rates and sweat trace mineral concentrations [18,20]. Furthermore, studies that made multiple comparisons of sweat trace mineral concentrations during heat exposure or exercise demonstrated lower sweat trace mineral concentrations over time despite fairly constant sweating rates over the same period [18,22].

Heat acclimation, which requires up to 10-14 days of daily heat exposure for optimal cardiovascular and thermoregulatory adaptations to hot environments [26], may also affect trace mineral concentrations and losses in sweat. Heat acclimation increases sweating rate and reduces sodium concentration [27]. Despite the limited availability of sweat trace mineral data in heat-acclimatized subjects, it appears that heat acclimation reduces sweat trace mineral content. The effects of 16 days of heat acclimation in 3

male subjects on sweat copper, iron and zinc losses have been studied [28,29]. The trace mineral losses were quantified from arm sweat following 7.5 hours of daily heat exposure. Arm sweat copper losses declined from 1.94 mg on days 5-8 to 1.04 mg during days 13-16 [28]. Sweat copper losses were not reported for days 1-4 of heat acclimation. An ~83% decline (13.7 mg to 2.18 mg) was observed in sweat zinc losses from the arm in these same 3 male subjects during the first few days after which the sweat zinc losses stabilized [28]. Consolazio *et al.* [29] reported mean arm sweat iron concentration values of ~0.36 mg/L during the first 12 days, which declined to 0.25 mg/L during the final 4 days. Because of the limited number of subjects used and no statistical comparisons made in these studies [28,29], deriving a conclusion about the effects of heat acclimation on sweat trace mineral concentration or losses is difficult. However, sweating rates appear to be higher and some trace mineral concentrations lower during exercise performed in the summer as compared to the winter season [30]. In addition, preliminary data from our laboratory from six males after a ten-day exercise-heat acclimation program concur with the earlier work by Consolazio *et al.* [28]. We observed a 3-fold decrease in arm sweat zinc concentration with only a ~16% higher sweating rate on day 10 versus day 1 of heat acclimation [unpublished observations]. Arm sweat from these same subjects showed no changes in sweat copper concentration or losses during the 10 days of heat acclimation. Whether or not these adaptations are the result of sweat dilution or trace mineral conservation requires additional study.

Many studies measuring trace minerals in sweat have attempted to correlate dietary intake of trace minerals to sweat concentrations or losses. However, no clear relationship between dietary trace mineral intake and sweat trace mineral concentrations or losses has been found [9,18,21,22,31]. Generally, no relationship between serum and sweat trace mineral concentrations or losses has been demonstrated [16,19,20,32], although it appears that that sweat mineral concentrations or losses may be related to whole body retention [32,33].

Sweat concentrations of trace minerals vary widely among collection sites [e.g., 10]. Most of the studies that have measured sweat trace mineral concentrations have collected sweat from various local body sites (e.g., back, arm). However, not only does sweat collected locally show considerable variability in trace mineral concentrations among regional body sites [10], regional trace mineral concentrations do not correlate with whole body sweat trace mineral concentrations and losses [6,34]. These observations between regional and whole body sweat have also been made for macrominerals [35], and some electrolytes [36,37]. For example, Cohn and Emmett [34] reported arm-bag sweat copper, iron, and zinc concentration values that were at least 2-fold higher as compared with whole-body sweat concentration values for these minerals. Jacob *et al.* [6] later attempted to correlate the trace mineral concentration of arm sweat collected using polyethylene arm bags to whole body sweat mineral losses. The trace mineral concentration of each arm resulted in a dramatic overestimation of whole body losses as compared to measured whole body losses, making it impossible to correlate trace mineral concentrations of arm sweat with whole body sweat losses. Further, the observed sweat zinc concentrations were highly variable between the right and left arm, suggesting variability or error in the collection technique. Aruoma *et al.* [10] also demonstrated variability in sweat copper, iron, and zinc concentrations simultaneously measured from different body regions during exercise in a temperate environment (Fig. 2). They observed sweat copper to range from 0.52 mg/L to 0.89 mg/L from four different sites. In addition, the authors reported variable sweat iron concentration values of 0.49±0.39 and 0.50±0.60 mg/L from the abdomen and chest and 0.28±0.14 mg/L and 0.20±0.18 mg/L from the arm and back, respectively. Lastly, Aruoma *et al.* [10] found sweat zinc concentration from the abdomen to be twice that of the back, arm, and chest (0.83±0.85 mg/L versus 0.48±0.56 mg/L, 0.44±0.48 mg/L, and 0.42±0.52 mg/L, respectively). One possible explanation for these regional variations in sweat trace mineral concentrations might be variations in the sweating rates at different body sites [38] and/or different evaporative rates at different body sites [39]. Therefore, it is plausible that there is a dilutive effect of sweat trace minerals at body sites with higher sweating rates or lower evaporative rates.

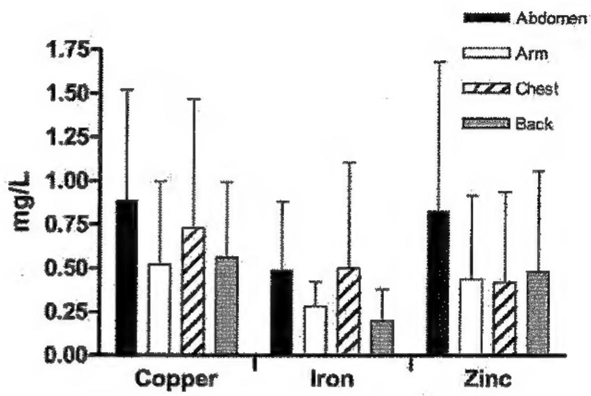

Fig. (2). Variations of sweat copper, iron, and zinc from different body sites during 30-40 min of exercise in a temperate environment. Data from Aruoma *et al.* [10].

It is important for researchers to consider the barriers associated with collecting uncontaminated sweat samples for accurate trace mineral analyses. These issues specifically relate to the introduction of external sources of trace mineral contamination of samples, sweat evaporation, sample leakage during collection, and obtaining sufficient volume for trace mineral analyses. Some of the earliest studies presented in this review reported high sweat trace mineral concentrations that were probably due to analytical interference or external contamination [8,24]. In addition, if the trace mineral content of cell-free sweat is of particular interest, then caution is warranted for sufficient skin site preparation to avoid epidermal trace mineral contamination. This is especially true when attempting to collect sweat for cell-free iron measurement; however, even the most thorough skin preparation may still not completely eliminate sweat gland duct-containing iron [17].

The evaporation of sweat, especially during whole-body sweat collection, is another potential problem that must be avoided in order to obtain accurate measurements of trace minerals in sweat since sweat evaporation increases the apparent concentration of dissolved mineral. The use of local sweat collection methods [37,40,41] reduces the probability of evaporation, but increases the likelihood of reduced sweating efficiency and hidromeiosis [37, 42,43], which could lead to increased sweat trace mineral concentrations. However, the potential for this limitation can be minimized by employing sweat collection periods of <60 minutes [43]. Local measures of sweat mineral concentrations and losses are also poorly correlated with whole body sweat mineral losses [6,44]. The methodological limitations of using whole body washdown techniques or similar methods have been well described [45,46]. Clever modifications to the whole body washdown technique have been proposed [46], but this method is complicated by the need for non-metal exercise equipment inside the plastic frame if trace minerals are of interest.

EFFECT OF SWEAT TRACE MINERAL LOSSES ON NUTRITIONAL REQUIREMENTS

Because of the widely variable sweat trace mineral data reported among studies discussed in the previous sections, there currently remains an important, unanswered question: Might sweat losses of trace minerals affect human requirements for the trace minerals? The Dietary Reference Intakes (DRI) are based on meeting the needs of normally active and healthy people [47]. However, nutrient needs of Soldiers [48], and those of athletes and workers exposed regularly to hot environments might be affected. It has been demonstrated that soldiers develop micronutrient deficiency disorders (namely iron) and that consumption of extra calories does not occur or is not effective in preventing micronutrient deficiency [49]. Further, it is unknown if substantial losses of trace mineral in sweat would impact whole body trace mineral retention or trace mineral absorption. Previous studies have shown absorption to be affected by dietary intake or whole body status for copper, iron, and zinc [50,51,52].

Copper

It is not known if the current dietary copper requirement for adults (0.90 mg/day) is adequate to replace sweat copper losses incurred through regular daily sweating; however, a few studies have shown that sweat copper losses may impact the dietary copper requirement in men [6,7,28]. Jacob *et al.* [6], suggested that whole body sweat copper losses in subjects under close supervision contributed 25-30% to the Recommended Dietary Allowance (1981 RDA = 1.2 mg/day). By the current DRI for copper (0.90 mg/day), the losses reported by Jacob *et al.* [6] would contribute 35-40% to the dietary copper requirement. Other studies, such as that conducted by Hoshi *et al.* [7], suggest that the whole body copper sweat losses under these conditions (30 min sauna) add only ~4% (0.039 mg copper) to the dietary copper requirement. Although continuous exposure to similar conditions and sweating rates imposed by Hoshi *et al.* [7] are highly unlikely for the general population, they are reasonable for Soldiers, athletes, and workers who are regularly exposed to arid climates. Losses incurred under such extreme conditions would increase the dietary copper requirement by 2-3 fold. Recall that Consolazio *et al.* [28] reported sweat copper losses from the arm of 1.04 mg during 7.5 hours of heat exposure during the final days of a heat acclimation program. These findings increase the dietary copper requirement by 100% and fall somewhat in line with results from Hoshi *et al.* [7].

Iron

It seems plausible that substantial losses of iron through heavy sweating together with inadequate dietary iron intake could have an important impact on a number of biological processes, including human performance; however, iron losses in sweat do not appear to affect the dietary iron requirement, especially when one considers the contribution of cellular iron loss. Green *et al.* [53] originally estimated dermal iron loss to be 0.24 mg/day in sedentary males and females. Vellar [16] studied whole body sweat iron losses in males during 1 hour of heat exposure and reported cell-free and cell-rich sweat iron losses of 0.38±0.14 mg/hr and 0.53±0.21 mg/hr with sweating rates of 1.25 L/hr. These results suggest that iron losses in sweat under continuous exposure to these conditions could potentially increase the dietary iron requirement by over 100% in males. In contrast, Wheeler *et al.* [21] reported whole body sweat iron loss to be ~4% (0.32 to 0.38 mg/day) of the dietary iron requirement for males under the conditions of their study – habitual activity with 2 hours of exercise/day in a warm environment. Results reported by Jacob *et al.* [6] concur with the whole body sweat iron losses observed by Wheeler *et al.* [21], where the authors found that whole body sweat iron losses might increase by 4% the dietary iron requirement for males. Brune *et al.* [17] found mean steady-state iron losses in whole body cell-free sweat to be 0.02±0.01 mg/L with a mean sweating rate of 1.16 L/hr while subjects bathed in a sauna for 30 minutes. Under these conditions, calculations suggest that whole body sweat iron losses would increase the dietary iron requirement for men by <1%.

Similar to zinc, the duration of physical activity and heat exposure need to be considered when estimating whole body sweat iron losses. Lamanca *et al.* [54] measured arm sweat iron losses in male and female runners during ~40 minutes of hot outdoor exercise. The arm sweat iron concentrations were significantly greater in the female runners (0.42±0.02 mg/L) versus the male runners (0.18±0.01 mg/L), but the calculated whole body sweat iron losses did not differ between the males and females. Consequently, the authors suggested that female athletes who perform 1 hour of daily exercise may need to increase their dietary intake of iron. Waller and Haymes [20] observed a 30-40% decrease in the estimated sweat iron losses from 30 to 60 minutes of exercise in males and females. Further, the combined 3 treatment conditions (heat-rest, heat-exercise, thermoneutral-exercise) resulted in an estimated whole body sweat iron loss of about twice that for males as compared to the females. Similarly, DeRuisseau *et al.* [22] found a ~50% decrease in both male and female mean arm sweat iron concentration during 2 hours of steady-state exercise in a thermoneutral environment. The authors estimated that the sweat iron losses over the 2-hour exercise period contributed to ~3% for the males and ~1% for the females of the dietary iron intake requirement. Finally, limited evidence suggests that chronic heat exposure may reduce sweat iron concentrations [29] which could potentially affect sweat iron losses. There is still much research required under a variety of environmental conditions and physical activity levels in order to accurately determine if sweat iron losses contribute significantly to the dietary iron requirement for males and females.

Zinc

The zinc losses in sweat may increase the dietary zinc requirement. Jacob *et al.* [6] measured whole body sweat zinc losses to be 0.50±0.38 mg/day. These losses contribute ~5% to the dietary zinc requirement of 11 mg/day in men. However, the losses reported by Jacob *et al.* [6] occurred in temperate environmental conditions with no reported physical activity levels. In the Hoshi *et al.* [7] study, volunteers had whole body sweat zinc concentrations of 0.37±0.38 mg/L with sweating rates of 1.1 L/hr which, during continuous exposure under the conditions of their study, would result in nearly a 100% increase in the dietary zinc requirement. Again, while exposure to similar extreme conditions are unlikely for the general population, they are reasonable for Soldiers, athletes and workers frequently exposed to hot conditions.

However, as demonstrated by DeRuisseau *et al.* [22], who observed declining sweat zinc concentrations over 2 hours of exercise in a temperate environment, it is unlikely that sweat zinc concentrations would remain constant over time in situations where physical activity/sweating is maintained for an extended duration. The authors reported that the experimental conditions in their study, (2 hours moderate exercise in thermoneutral conditions), would impose a dietary requirement increase for zinc by 8-9% for men and women. During the heat acclimation program study by Consolazio *et al.* [28], heat acclimation reduced the arm sweat zinc losses from 13.7 mg/day to ~2.25 mg/day. Therefore, in situations of increased acute physical activity levels and/or chronic heat exposure, the dietary zinc requirement may need to be increased, but an overestimate of the dietary zinc requirement is possible without consideration of the effect on sweat zinc losses from these two conditions. Additional studies examining sweat zinc losses over longer durations with increased physical activity and heat exposure are necessary to accurately determine the need of dietary zinc requirements in these situations.

SUMMARY

Copper, iron, and zinc are nutritionally essential trace elements that are required for numerous biological functions. Excessive losses of these trace minerals through sweat may affect their nutritional requirement. Data presented in this review suggest that the dietary requirements for copper and zinc, but not iron, may be affected by their losses in sweat under certain environmental conditions. However, variability between studies due to differences in analytical methods, collection sites, and environmental controls make it difficult to draw firm conclusions on the impact of sweating on trace mineral losses. Future studies should focus on minimizing experimental error through the use of carefully controlled environmental conditions, the choice of appropriate local collection sites, and the use of modernized analytical equipment. Whole body sweat collection is the preferred method in determining accurate trace mineral concentrations and losses. However, whole body sweat collection is impractical and modified methods may not be well suited for trace mineral analysis. It therefore seems desirable to establish a corollary of local trace mineral sweat concentrations with whole body trace mineral sweat concentrations and/or losses. Lastly, studies should focus on determining the effect of habitual sweating, prolonged physical activity, and heat acclimation on sweat trace mineral concentrations and losses, as individuals exposed to these types of activities could be most prone to clinical or subclinical nutritional deficiencies due to increased sweat losses.

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REFERENCES

[1] Stauber JL, Florence TM. A comparative study of copper, lead, cadmium and zinc in human sweat and blood. Sci Tot Envir 1988; 74: 235-47.

[2] Sato K, Sato F. Sweat secretion by human axillary apoeccrine sweat gland *in vitro*. Am J Physiol 1987; 252: R181-R187.

[3] Keen CL, Hanna LA, Lanoue L, *et al*. Developmental consequences of trace mineral deficiencies in rodents: Acute and long-term effects. J Nutr 2003; 133: 1477S-80S.

[4] Uriu-Adams JY, Keen CL. Copper, oxidative stress, and human health. Mol Aspects Med 2005; 26: 268-98.

[5] Mitchell HH, Hamilton TS. The dermal excretion under controlled environmental conditions of nitrogen and minerals in human subjects, with particular reference to calcium and iron. J Biol Chem 1949; 178: 345-61.

[6] Jacob RA, Sandstead HH, Munoz JM, Klevay LM, Milne DB. Whole body surface loss of trace metals in normal males. Am J Clin Nutr 1981; 34: 1379-83.

[7] Hoshi A, Watanabe H, Kobayashi M, *et al*. Concentrations of trace elements in sweat during sauna bathing. Tohoku J Exp Med 2001; 195: 163-69.

[8] Hohnadel DC, Sunderman Jr. FW, Nechay MW, McNeely MD. Atomic absorption spectrometry of nickel, copper, zinc, and lead in sweat collected from healthy subjects during sauna bathing. Clin Chem 1973; 19: 1288-92.

[9] Turnland JR, Keen CL, Smith RG. Copper status and salivary copper in young men at three levels of dietary copper. Am J Clin Nutr 1990; 51: 658-64.

[10] Aruoma OI, Reilly T, MacLaren D, Halliwell B. Iron, copper and zinc concentrations in human sweat and plasma; the effect of exercise. Clin Chim Acta 1988; 177: 81-8.

[11] Omokhodion FO, Howard JM. Trace elements in the sweat of acclimatized persons. Clin Chem Acta 1994; 231: 23-8.

[12] Saraymen R, Kiliç E, Süleyman Y. Sweat copper, zinc, iron, magnesium and chromium levels in national wrestler. İnönü Üniversitesi Tip Fakültesi Dergisi 2004; 11(1): 7-10.

[13] Saraymen R, Kiliç E, Süleyman Y. Magnesium, copper, zinc, iron, and chromium levels in sweat of boxers. İnönü Üniversitesi Tip Fakültesi Dergisi 2003; 10(3): 121-5.

[14] Brock, JH, Djeha A, Ismail M, Oria R, Sinclair RH. Cellular responses to iron and iron compounds. Adv Exp Med Biol 1994; 356: 91-100.

[15] Mascotti, DP, Rup D, Thach RE. Regulation of iron metabolism: translational effects mediated by iron, heme, and cytokines. Annu Rev Nutr 1995; 15: 239-61.

[16] Vellar OD. Studies on sweat losses of nutrients I: Iron content of whole body sweat and its association with other sweat constituents, serum iron levels, hematological indices, body surface area, and sweat ratethe influence of an oral iron load on the iron content of whole body cell-free sweat. Scand J Clin Lab Invest 1968; 21: 157-67.

[17] Brune M, Magnusson B, Persson H, Hallberg L. Iron losses in sweat. Am J Clin Nutr 1986; 43: 438-43.

[18] Tipton K, Green NR, Haymes EM, Waller M. Zinc loss in sweat of athletes exercising in hot and neutral temperatures. Int J Sport Nutr 1993; 3: 261-71.

[19] Paulev PE, Jordal R, Pederson NS. Dermal excretion of iron in intensely training athletes. Clin Chim Acta 1983; 127: 19-27.

[20] Waller MF, Haymes EM. The effects of heat and exercise on sweat iron loss. Med Sci Sports Exerc 1996; 28: 197-203.

[21] Wheeler E, El-Neil H, Willson JOC, Weiner JS. The effect of work level and dietary intake on water balance and the excretion of sodium, potassium, and iron in a hot climate. Br J Nutr 1973; 30: 127-37.

[22] DeRuisseau KC, Cheuvront SN, Haymes EM, Sharp RG. Sweat iron and zinc losses during prolonged exercise. Int J Sports Nutr Exerc Metab 2002; 12: 428-37.

[23] Lukaski H. Vitamins and minerals. In: Wolinsky I, Driskell JD, Eds, Handbook of sports nutrition. Boca Raton, FL, CRC Press. 1996; 157-73.

[24] Seutter E, Sutorius AHM. The quantitative analysis of some constitutents of crude sweat. Dermatologica 1972; 145: 203-9.

[25] Stolwijk JAJ, Saltin B, Gagge AP. Physiological factors associated with sweating during exercise. Aerospace Med 1968; 39: 1101-5.

[26] Pandolf KB, Young AJ. Environmental extremes and performance. In: Shepard RJ, Astrand PO, Eds, Endurance and sport. Oxford, Blackwell. 1992; 270-82.

[27] Allan, JR, Wilson, CG. Influence of acclimatization on sweat sodium concentration. J Appl Physiol 1971; 30: 708-12.

[28] Consolazio CF, Nelson RA, Matoush LO, Hughes RC. The trace mineral losses in sweat. Denver, CO: U.S. Army Medical Research and Nutrition Laboratory, Report No. 284, 1964.

[29] Consolazio CF, Matoush LO, Nelson RA, Harding RS, Canham JE. Excretion of sodium, potassium, magnesium, and iron in human sweat and the relation of each to balance and requirements. J Nutr 1963; 407-15.

[30] Hoshi A, Watanabe H, Chiba M, *et al*. Seasonal variation of trace element loss to sweat during exercise in males. Environ Health Prev Med 2002; 7: 60-3.

[31] Vellar OD. Studies on sweat losses of nutrients II: the influence of an oral iron load on the iron content of whole body cell-free sweat. Scand J Clin Lab Invest 1968; 21: 344-6.

[32] Milne DB, Canfield WK, Mahalko JR, Sandstead HH. Effect of dietary zinc on whole body surface loss of zinc: impact on estimation of zinc retention by balance method. Am J Clin Nutr 1983; 38: 181-6.

[33] Prasad AS, Schulert AR, Sandstead HH, Miale Jr A, Farid Z. Zinc, iron, and nitrogen content of sweat in normal and deficient subjects. J Lab Clin Med 1963; 62: 84-9.

[34] Cohn JR, Emmett EA. The excretion of trace metals in human sweat. Ann Clin Lab Sci 1978; 8: 270-5.

[35] Palacios C, Wigertz K, Weaver CM. Comparison of 24-hour whole body versus patch tests for estimating body surface electrolyte losses. Int J Sports Nutr Exerc Metab 2003; 13: 479-88.

[36] Patterson MJ, Galloway SDR, Nimmo MA. Variations in regional sweat composition in normal human males. Exp Physiol 2000; 85: 869-75.

[37] van Heyningen R, Weiner JS. A comparison of arm-bag sweat and body sweat. J Physiol 1952; 116: 395-403.

[38] Nadel ER, Mitchell JW, Saltin B, Stolwijk JAJ. Peripheral modifications to the central drive for sweating. J Appl Physiol 1971; 31: 828-33.

[39] Park SJ, Tamura T. Distribution of evaporation rate on human body surface. Ann Physiol Anthrop 1992; 11: 593-609.

[40] Boysen TC, Yanagawa S, Sato F, Sato K. A modified anaerobic method of sweat collection. J Appl Physiol 1984; 56: 1302-07.

[41] Brisson GR, Boisvert P, Peronnet F, *et al*. A simple and disposable sweat collector. Eur J Appl Physiol 1991; 63: 269-72.

[42] Candas V, Libert JP, Vogt JJ. Sweating and sweat decline of resting men in hot humid environments. Eur J Appl Physiol Occup Physiol 1983; 50: 223-34.

[43] Collins KJ, Weiner JS. Observations on arm-bag suppression of sweating and its relationship to thermal sweat-gland "fatigue." J Physiol 1962; 49: 254-61.

[44] Palacios C, Wigertz K, Martin B, Weaver CM. Sweat mineral loss from whole body, patch, and arm bag in white and black girls. Nutr Res 2003; 23: 401-11.

[45] Dill DB, Jones BF, Edwards HT, Oberg SA. Salt economy in extreme dry heat. J Biol Chem 1933; 100: 755-67.

[46] Shirreffs SM, Maughan RJ. Whole body sweat collection in humans: an improved method with preliminary data on electrolyte content. J Appl Physiol 1997; 82: 336-41.

[47] Barr SI, Murphy SP, Poos MI. Interpreting and using the dietary reference intakes in dietary assessment of individuals and groups. J Am Diet Assoc 2002; 102:780-8.

[48] Institute of Medicine. Military dietary reference intakes: process to establish, uses, and delivery methods. Mineral requirements for military personnel. Washington, D.C., National Academy Press. 2006; 36-57.

[49] McClung JP, Marchitelli LJ, Friedl KE, Young AJ. Prevalence of iron deficiency and iron deficiency anemia among three populations of female military personnel in the US Army. J Am Coll Nutr 2006; 25(1): 64-9.

[50] Hallberg L, Hulten L, Gramatkovski E. Iron absorption from the whole diet in men: how effective is the regulation of iron absorption? Am J Clin Nutr 1997; 66: 347-56.

[51] Lee DY, Prasad AS, Hydrick-Adair C, Brewer G, Johnson PE. Homeostasis of zinc in marginal human zinc deficiency – role of absorption and endogenous excretion of zinc. J Lab Clin Med 1993; 122: 549-56.

[52] Turnlund JR, Keyes WR, Anderson HL, Acord LL. Copper absorption and retention in young men at three levels of dietary copper by use of the stable isotope 65Cu. Am J Clin Nutr 1989; 49: 870-8.

[53] Green R, Charlton R, Seftel H, *et al.* Body iron excretion in man. Am J Med 1968; 336-53.

[54] Lamanca JJ, Haymes EM, Daly JA, Moffatt RJ, Waller MF. Sweat iron loss of male and female runners during exercise. Int J Sports Med 1988; 9: 52-5.

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